2 February 1973, Volume 179, Number 4072 SCIENCE

Diffusion and Chemical Transformation

An interdisciplinary excursion

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The chemical transformation of molecules takes place in an endless number of systems, natural and man-made. The rate and effectiveness of these transformations are influenced by the availability of the reactants. As transformation occurs, the original concentration of the reactants is depleted and, nearly always, is replenished by some process of diffusion. The net attainable speed of the reaction thus depends on the relative competition of reactivity and of the capability for diffusive flow in the relevant parts of the system. Processes are encountered in nearly all scientific "disciplines," and in everyday life, where the interaction of diffusional transport and a transformation reaction determine or limit the workability of a phenomenon. Only space limits the number of examples that could be enumerated, from geology, agronomy, or physiology to the dyeing of garments or the pot on the kitchen stove.

Some 10^{10} grams of hydrocarbon molecules undergo catalytic conversion every hour in the petroleum industry of North America. It is significant that the magnitude of this molecular traffic just about equals that of food and oxygen molecules that undergo metabolic transformation within the human population of North America.

It is intriguing and most instructive to recognize the very general and therefore basic applicability of the laws that describe the diffusion-transformation interaction, and to trace their implications across many disciplines. I and my colleagues began to examine the basic features of this interaction in efforts to determine its role in the industrial processes for the conversion of hydrocarbons in petroleum.

Effectiveness Factor of Chemical Engineering Science

In 1939, at the 96th meeting of the American Chemical Society, E. W. Thiele (*1*) presented a convincing mathematical analysis of the interaction between reactivity and diffusive flow in porous catalyst particles. Zeldovitch (*2*) in the Soviet Union, and Damköhler (*3*) in Germany had published results of similar studies. They showed that the actual attainable reaction rate drops below that corresponding to the intrinsic reactivity by an amount η, called the effectiveness factor, dependent on a dimensionless factor φ. This factor represents a combination of the true reaction rate constant k of the material, its geometric size R, and the diffusivity D, of the molecules therein.

Figure 1 shows the results of mathematical solutions of the diffusion-transformation equations for first order kinetics and spherical particle shape, and for the first and second order cases of kinetics and flat plate geometry. Thiele's analysis demonstrated that only in situations where the combination of parameters in φ becomes greater than unity must we consider the modifying influence of these parameters on the performances of the system, at least for the three examples solved mathematically.

There were obviously an endless number of variants for which the functional forms of the effectiveness factor could be derived, such as for other shapes of particles, for various forms of the reaction kinetics, or for the presence or absence of changes in molecular volume. We became interested in a more general question: Where and when should the diffusion determining parameters—size and diffusivity—be considered relevant and influential? Where would they or would they not influence the design, manipulation, or behavior of the catalytically active material? For example, did they influence or determine the operating behavior of a Thermofor catalytic cracking (TCC) unit, where pearl-sized catalyst particles were used to transform heavy petroleum fractions to the hydrocarbons of gasoline?

An Interdisciplinary Theorem

Unfortunately, the use of Thiele's method required some knowledge of k, that is, it was necessary to know what the intrinsic kinetic rate would be in the absence of the diffusional effects; the very effects whose existence or absence we wished to ascertain.

In 1943, Wagner (*4*) demonstrated that the Thiele derivation for first order kinetics could be transformed to contain the actual rate instead of the chemical rate constant. This was an

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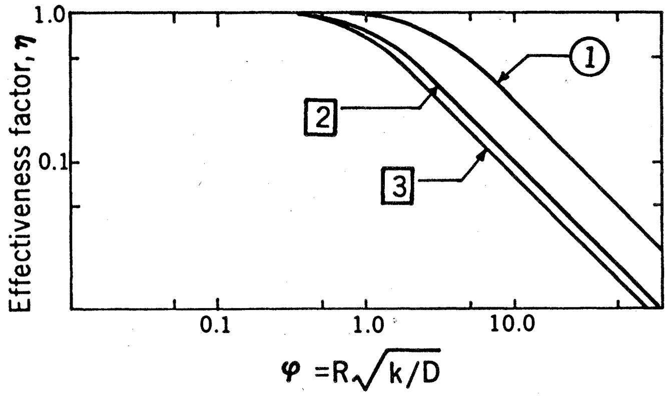


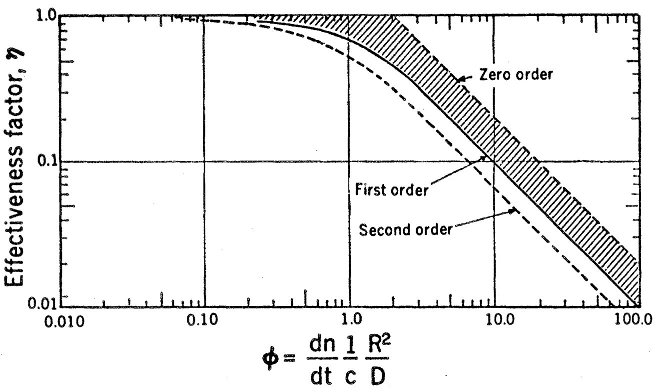


Fig. 1 (left). The Thiele effectiveness factor for a catalytically active volume, expressing how effectively the diffusion supply of molecules supports the intrinsically available reaction rate. Curve 1, first order kinetics in spherical particle geometry; curves 2 and 3, first and second order kinetics in flat plate geometry. Fig. 2 (right). The effectiveness factor expressed in terms of only "observable" parameters contained in the composite parameter Φ. The shaded area contains all solutions for Langmuir (or Michaelis-Menten) kinetics.

important step. We were able to show (*5*) that the Thiele effectiveness factor could always be related to a parameter containing only observable quantities like the actual reaction rate. We later (*6*) termed this parameter Φ, the use of which has now become widespread. Figure 2 shows the functional course of the effectiveness factor (for first and second order kinetics) in terms of this parameter:

$$\Phi = (dn/dt)\ (1/c)\ (R^2/D)$$

where dn/dt is the actual, observed, reaction rate per unit volume of the catalyst particles, c is the externally applied reactant concentration, R is size in terms of an approximate equivalent particle radius, and D is the diffusivity of the reactant in the particle medium.

Using Φ we were also able to formulate (*5*) a general criterion useful for orientation in any system, even in the absence of detailed information on particle shape and chemical kinetics. A significant diffusional modification would be expected if Φ approached or exceeded the region of unity, with an uncertainty of less than half an order of magnitude up or down, that is, if

$$\Phi = (dn/dt)\ (1/c)\ (R^2/D) \geqq 0.3 \ldots 3$$

Among the various specific mathematical solutions supplied were those of Roberts and Satterfield (*7*) and Schneider and Mitschka (*8*). These workers provided solutions for the large spectrum of cases described by Langmuir-Hinschelwood kinetics. These solutions are notable for two reasons: first, the entire set of solutions for Langmuir kinetics, $dn/dt = kc/(1 + Kc)$, in which the reactant adsorption constant K can have any value from zero to infinity, fall into the shaded area of Fig. 2; second, Langmuir-Hinschelwood kinetics have concepts, meaning, and format in common with the Michaelis-Menten kinetics used by the biochemist. Biochemists and chemical engineers could thus make good use of each other's efforts and knowledge.

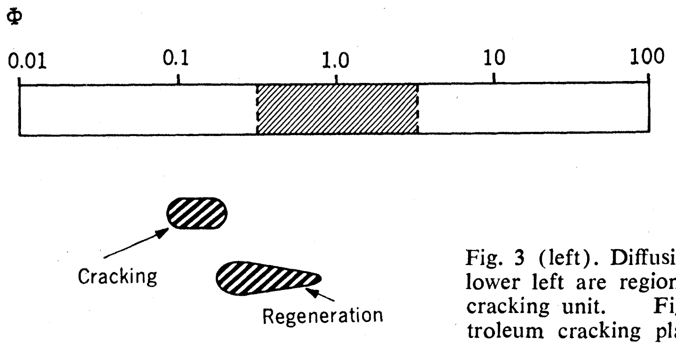
Process Research, Engineering, and Investment Guidance

The Φ criterion proved invaluable in the pursuit of research as well as in the practice of catalysis. For example, we received some early guidance concerning the above-mentioned question concerning the operating behavior of the catalyst beads in the petroleum cracking process. When we introduced the numerical values relevant to the TCC process into the Φ criterion, we determined that Φ was safely below unity in the cracking cycle (Fig. 3); but in the regeneration cycle, however, the reaction of oxygen with carbon deposits was always close to the critical region, and sometimes well into it, in the high-temperature portion of the adiabatic regeneration kiln.

Because of this borderline situation, we did develop the more detailed mathematical expressions for the regeneration kinetics of catalyst particles (*9*). With these, models of the behavior of full-scale TCC regeneration kilns were constructed by my colleagues Prater *et al.* (*10*) and Weekman *et al.* (*11*). Hundreds of design and operating modifications were explored, a task that would have been impossible by actual engineering testing or empirical calculation.

The phenomenon of diffusion inhibition encountered during portions of the regeneration cycle had other practical consequences. It could create internal mechanical strains in the catalyst particles and thereby contribute to catalyst attrition losses through breakage (*12*). My colleagues modified the internal structure of the catalyst particles by incorporation of a bimodal pore system (*13*), and thereby increased the diffusivity of the catalyst sufficiently to shift Φ largely out of the range of diffusion control (*12*). The modified catalyst material thus remedied these attrition losses (*14*), as shown in Fig. 4.

The Φ criterion provided us with further guidance. We discovered that a new family of zeolite cracking catalysts could provide us with per-unit-volume reactivities for hydrocarbon splitting of as much as a factor of 2,000 to 10,000 (*15*) above the level of conventional catalysts. Clearly, any future commercial utilization of such an increase in dn/dt for the pearl-sized particles would move the operating mode far into the undesirable diffusional regime of Φ. Since materials science offers no way to further increase D, the diffusivity of the porous catalyst particles, by any appreciable factor, the only manner available to bring the magnitude of Φ below unity is the reduction of particle size R. This clearly pointed to the use of the fluidized particle technology for future zeolite cracking process developments if they were to utilize high catalyst activities. This engineering technology uses particles of less than about 0.1 millimeter in diameter. For the Φ criterion, this makes R 2,000 times smaller than in the case of the beads of the TCC process! Indeed, with the newer



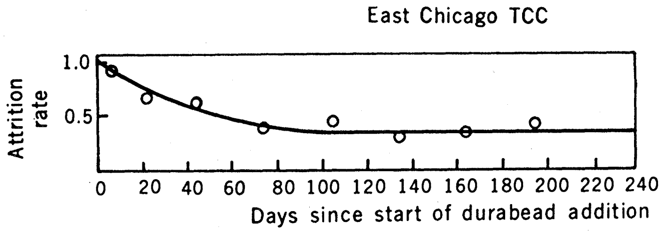


Fig. 3 (left). Diffusion inhibition occurs when Φ is in or beyond the shaded area. At lower left are regions of operation encountered in the catalysts of a TCC petroleum cracking unit. Fig. 4 (right). Improvement of mechanical attrition losses in a petroleum cracking plant, resulting from improved diffusivity in catalyst spheres from 0.007 to 0.013 cm^2/sec (*14*). Gradual replacement of the old catalyst more than halved catalyst consumption.

catalysts, the transition to fluidized units is now well under way.

The use of the Φ criterion in kinetic studies became standard laboratory practice. The importance of such guidance was well illustrated by a comment by Wei (*16*) who stated that some 30 percent of kinetic results reported at the 1960 International Congress of Catalysis were probably distorted by diffusional effects.

The generality of the applicability of the Φ criterion was subjected to much critical examination. Austin and Walker (*17*) and Peterson (*18*) showed that diffusion effects can set in at Φ values far below $\Phi \approx 1$ in the case of strong poisoning of the catalyst by the reaction product.

In practice, the occurrence of such strong product poisoning is rare, and can usually be detected by the experienced practitioner by way of unusual behavioral symptoms. If this important point of caution is taken into account, a more precise statement of the Φ criterion is: When Φ is greater than 1, the influence of diffusion parameters *must* be considered; if Φ is less than 1, the system may be assumed to be performing at its maximum chemical conversion capacity, except in rare instances of strong product poisoning.

Cells, Enzymes, and Spermatozoa

The microbial cell represents a chemical reactor. In fact, it can be described as a particle composite of many catalysts. Oxygen, if it is to be metabolized, must diffuse into the cell. For some time, microbiologists have suspected that internal diffusion inhibition plays a decisive role in microbial respiration (Fig. 5A). Longmuir (*19*) and Johnson (*20*) have shown that diffusion can become a controlling factor in yeast cells under conditions of oxygen starvation, and in particularly large unicellular organisms such as *Bacillus megatorium*. The Φ criterion, when applied to Longmuir's and Johnson's studies, confirms this. It also demonstrates the effect of low oxygen concentration *c* and of the cell size *R* on the onset of diffusion inhibition. We have made much use of the criterion in developing technology for producing proteins from petroleum by yeast fermentation.

More recently, much attention has been given to the reactivity of enzymes mounted in porous polymeric solids (Fig. 5B). Does the mounted enzyme entity equal the dissolved enzyme molecule in intrinsic chemical activity? Superficially, the measured rates do not always so indicate. In investigating this problem, biochemists have repeated mathematical derivations along the line of Thiele's treatment for the case of the Michaelis-Menten kinetics (*21*, *22*). We have noted before that the requisite mathematical solutions were already available as developed for the synonymous Langmuir kinetics (*7*, *8*). Actually, the simple Φ criterion is sufficient to define the conditions involving the activity level and the polymer dimensions, for which the measured rates can be interpreted as true intrinsic rates. With such precautions, it is found that these intrinsic molecular reactivities are equivalent to those of many enzymes in solution.

There has been an analogous inquiry into the chemical reactivity of crystals of enzymes compared with their dissolved counterparts (Fig. 5C). Sluyterman and deGraaf (*23*) again made a full and independent Thiele-type derivation in analyzing their results; but the Φ criterion is adequate to show that the crystals of several hydrolytic enzymes have normal enzyme activity provided that they are not grown to too large a size.

A more lively subject of discussion is diffusion in the tail of the spermatozoon, for it, too, is an important chemical reactor (Fig. 5D). Along the whole length of the tail of the spermatozoon the energy for the wiggling motion of propulsion is derived from hydrolysis of adenosine triphosphate (ATP). But ATP is produced in the body near the anterior end of the tail.

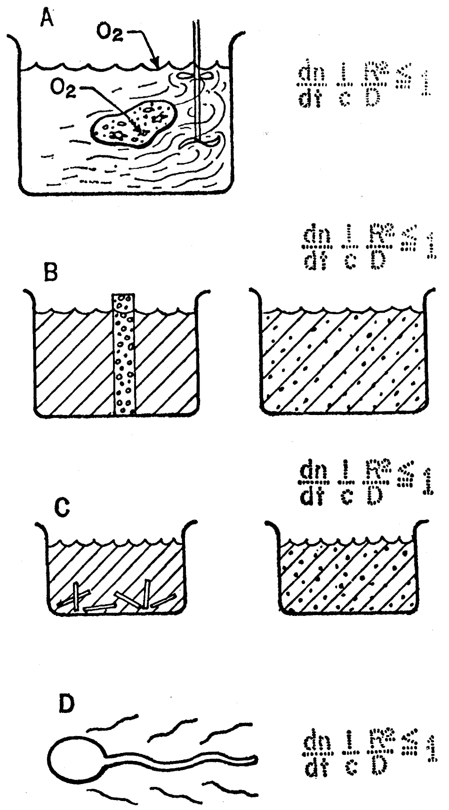


Fig. 5. The occurrence of analogous problems that involve the interaction of molecular reaction and diffusion. (A) The growth rate of microorganisms may be subject to diffusion inhibition [after Longmuir (*19*) and Johnson (*20*)]. (B) Kinetics of polymer-mounted enzymes [after Hornby *et al.* (*21*) and Goldman *et al.* (*22*)]. (C) Reactivity of enzyme crystals compared to enzymes in solution [after Sluyterman and deGraaf (*23*)]. (D) Optimum length of tail of a spermatozoon [after Nevo and Rikmenspoel (*24*)].

The question of whether the minute concentration of ATP produced in that area is sufficient to reach the entire length of the tail, by diffusion, was investigated by Nevo and Rikmenspoel (*24*). They again performed a Thiele-type mathematical derivation, for zero order kinetics, and concluded that the ATP concentration was adequate to provide transport by diffusion. It is interesting to turn the question around, and to apply the simple Φ criterion to determine how long the tail could be before there would be a chemically useless portion in its design. If we use the data of Nevo and Rikmenspoel for the rate, the ATP concentration, and diffusion coefficient, we find that 5×10^{-3} to 9×10^{-3} centimeter is the length of tail that could be effectively utilized. We also find that the spermatozoa have anticipated us, since they have grown their tails to just 5×10^{-3} centimeter.

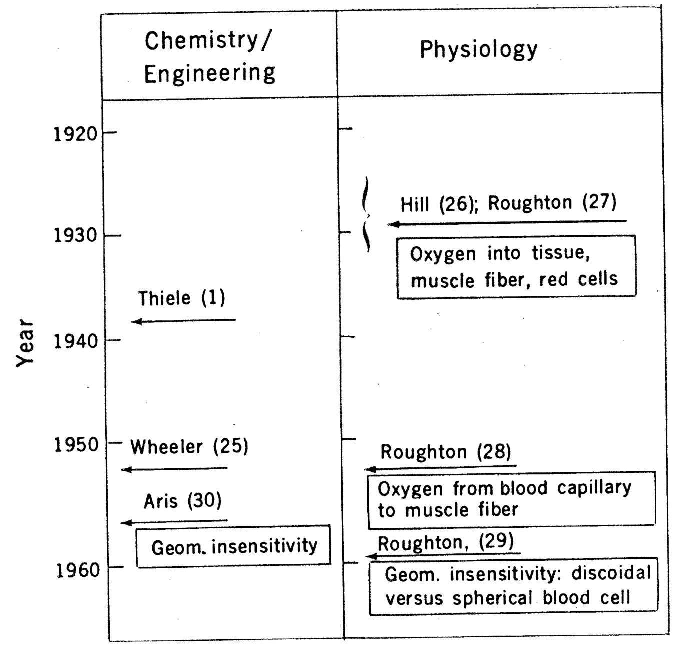
Engineering Design, Evolution, and Physiology

This precise approach to optimum design is impressive; the work on yeasts also implied that the living cell is usually just small enough to avoid diffusion problems during oxygen metabolism at normal oxygen pressures. When we first calculated the critical size of catalyst particles for the TCC cracking processes, we were surprised to find that, in the course of evolution of this process, one had somewhat empirically arrived at a catalyst particle size just large enough for optimum utilization. We have concluded that these various but analogous achievements are not accidental. Evolution tends to arrive at optimal design by selection. Given sufficient time, engineering process development in a competitive world is also an evolutionary process with all forces working for survival of the fittest components, analogous to the evolution of biological machinery. The term competitive need not imply any particular man-made economic system, since the finiteness of space, resources, and human lifetime alone produces the natural bases for a competitive system.

Because the diffusion-transformation phenomena are so important in optimal reactor design, it seems probable that scientists interested in biological processes recognized early the need to examine this phenomenon. It is revealing to examine some of the investigations undertaken by physiologists some years ago.

Ten years before the work of Thiele, and 20 years before Thiele's calculations were extended to zero order reactions by Wheeler (*25*), both Hill (*26*) and Roughton (*27*) had produced similar mathematical derivations for zero order kinetics in slab geometry (Fig. 6). They applied their derivations to such questions as the depth of tissue from its source of oxygen in which normal metabolism could be sustained, internal diffusion inhibition in the metabolic processes of the red blood cells, and myoglobin metabolism in muscle fibrils. By 1952, Roughton (*28*) had extended such derivations to situations as complex as reactions between two concentric cylinders, with both a zero *and* a first order reaction simultaneously involving the diffusing species. This was of interest in an understanding of the overall process of oxygen transfer from a blood capillary to a nearby muscle fiber where oxygen is consumed.

For a long time physiologists observed that at certain times the spherical erythrocytes of the blood would take on a biconcave discoidal shape. It was suggested that the biconcave shape might be more favorable for minimizing internal diffusion inhibition or, in the language of chemical engineers, it might give a better Thiele effectiveness factor. In 1960, Roughton (*29*), after making many detailed calculations, concluded that the effectiveness factor was almost insensitive to such changes in shape. A point of interest is that, in chemical engineering circles there had evolved a collection of purely mathematical studies, such as those of Aris



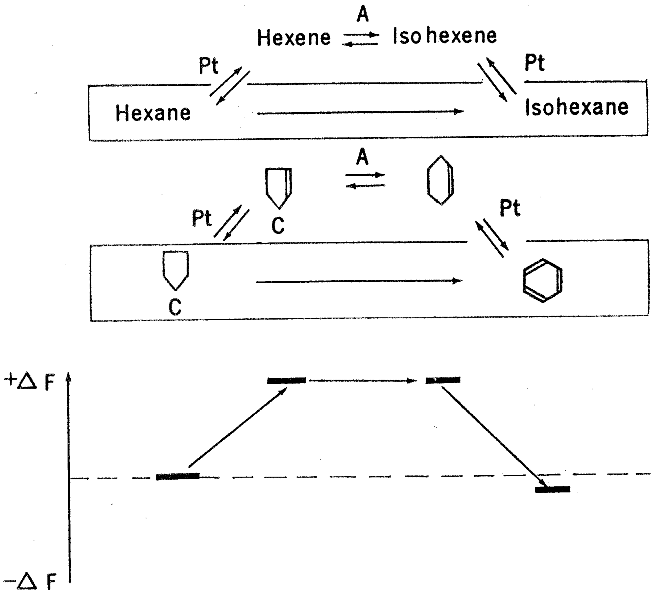
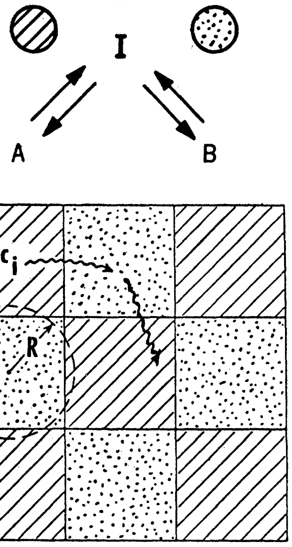


Fig. 6 (left) The separate quest of the analogous problem in different scientific disciplines. Workers were studying independently the effect of the interaction of chemical kinetics and diffusion transport, in systems of similar geometry. Fig. 7 (right). Polystep reactions in the catalytic transformation of hydrocarbon structures, as practiced by the petroleum industry. Paraffin isomerization (above) and aromatization of alkylcyclopentanes are carried out over catalysts that contain both acidic sites (*A*) and platinum (*Pt*). The free-energy changes in the reaction sequence are qualitatively similar, and involve a high-energy intermediate.



$$\frac{dn}{dt}\,\frac{1}{C_i}\,\frac{R^2}{D} < 1$$

$$C_i \approx K_{AB}\left[A\right]$$

Fig. 8. The intimacy criterion applied to the two-step reaction *A* to *B*, catalyzed by geometrically separate catalytic regions, with an intermediate *I* required to travel by diffusion from one type of catalyst to another.

(*30*), that were quite detached from specific physical problems, and that demonstrated a high degree of insensitivity of diffusion calculations to that type of variation in geometry. It is evident that the physiologists and chemical engineers concerned with these problems were unaware of each other's work and progress.

Polystep Chemistry

Another large-scale industrial catalytic process is that of gasoline reforming. In this process an initial mixture of gasoline-range hydrocarbons is converted to a mixture of hydrocarbons having adequate octane number. The major chemical objective is to induce skeletal branching and aromatization of the hydrocarbons. Examples are the conversion of *n*-heptane to isoheptanes, and the transformation of alkylcyclopentane srtuctures into alkylbenzenes. Certain platinum-containing and acidic aluminas have always been used as the catalytic solids for these conversions. Early in the history of the use of these catalysts it was suggested by Mills *et al.* (*31*) that they catalyze by way of intermediate olefinic species, as shown in Fig. 7. It occurred to us that if such intermediate species were formed as true desorbed molecules, we could gain a new degree of freedom in catalyst design. If the molecules of the intermediate species could diffuse rapidly enough between two different catalyst compositions that catalyze the separate reaction steps, we could design composite catalyst materials containing different solids to catalyze the various reaction steps. However, the proposed intermediate reaction step represented a thermodynamically unfavorable transformation with a positive change in free energy (Fig. 7). The diffusion intermediates, if they were indeed operative, would be present in very low concentration, perhaps so low as to be undetectable.

The Φ diffusion criterion proved applicable to this problem (*32, 33*) with the term for concentration now representing the maximum possible—although very small—concentration c_i of the intermediate species I (Fig. 8). The symbol *R* is now the approximate radius of each *component* particle or region. It is a measure for the average distance the intermediate species must diffuse in order to travel between the two catalytic components. It was interesting to find that the relatively simple concepts that lead to the Φ criterion for reaction intermediates lead to a direct link between the feasibility of a rate process and a purely thermodynamic property, namely the free energy of formation of the intermediate species which determines the maximum attainable concentration c_i. Furthermore, it was a pleasant surprise to find that the use of composited catalytic materials should be perfectly practicable, even for intermediates whose formation would require a large positive change in free energy. The catalyst component particles would be manageably small, with *R* of 1 micrometer or more.

In due course, we were able to demonstrate (*33, 34*) the operability of the principle of composited polystep catalysts. For example, a simple mechanical mixture of acidic solid particles and of platinum-containing particles successfully accomplished the reactions familiar to the reforming catalysts if the components were smaller than about 90 micrometers in size. The experiments, such as the one shown in Fig. 9 with *n*-heptane, confirmed this beautifully. Other hydrocarbon reactions were similarly accomplished, such as the hydrogenative splitting ("hydrocracking") of paraffins and the aromatization of alkylcyclopentanes.

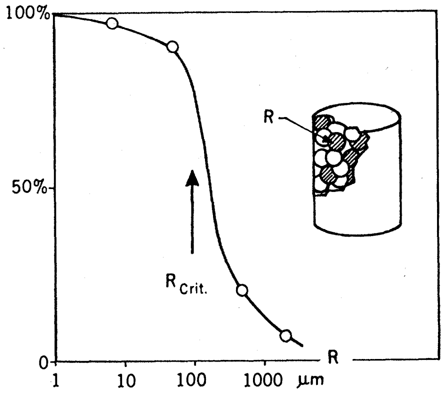


Fig. 9. Early demonstration of the application of the intimacy criterion for the polystep reaction of *n*-heptane isomerization over a mixture of highly porous platinum- and acid-bearing particles. Approach to theoretical (equilibrium) conversion (ordinate) depends critically on the component particle size expressed by their radius *R*.

These experiences vividly confronted us with the realization that a piece of catalytically effective material may have substructure and can be an intricate catalytic apparatus in its own right. Furthermore, because of the basic generality and applicability to any polystep reaction systems of the Φ criterion, it should also apply to the most intricate catalytic apparatus of nature, the living cell; to its various localized enzyme systems, such as the mitochondria, ribosomes, and other organelles; and to their substructures.

Polystep Biochemistry

For the metabolism of oxygen in the cellular substance the magnitude of the reaction rate is well known. In the steady state, this rate must characterize not only the rate of oxygen consumption, but also each step of the sequence of many sequential reactions. For any reaction rate, the Φ criterion should relate (*33, 35*) the maximum size of a cellular component such as a mitochondrion, which is to effectively convert a reaction intermediate, to the concentration of that intermediate. Also, concentration should be related to the free energy of formation of the compound. The result of such a calculation, based on the rate of oxygen metabolism of 10^{-8} mole per second per cubic centimeter, is shown in Fig. 10. The concentration of the intermediate substance (left ordinate) determines the maximum size of the enzymatic apparatus. Typical sizes of some cellular components are given for comparison. It is interesting that the typical concentration of cellular cytochrome c, about 10^{-8} mole/liter, also corresponds to the typical size of the whole cell. If an enzyme is assumed to be optimally utilized (a reasonable assumption for many situations) we can also relate the turnover number (right ordinate) to the size or intimacy parameter (*35*).

Some of the conclusions that can be drawn from this relationship (Fig. 10) are exemplified by the following. (i) Localized enzymes with turnover numbers approaching millions must be coupled to other cellular machinery having dimensions no greater than 20 to 80 μm, characteristic of the cristae or the ribosomes. (ii) Enzymes with higher turnover rates are likely to be discovered in yet smaller structural units, including such enzymes as may be involved in intramembrane processes. (iii) Within cell membranes, effective reaction intermediates (and enzymes) at concentrations as minute as 10^{-15} mole/liter, some seven orders of magnitude below the cellular concentration of cytochrome c, may couple reaction steps on opposite sides. They can truly constitute high-energy thermodynamic species!

This analysis applies to reaction steps involved in the main sequence of the total oxygen consumption rate, and the concentrations are defined as molar quantities referred to the total cellular volume. A more sophisticated analysis to characterize the local environment of a certain type of subunit involved in a given chemical transformation must rely on the refined criterion for diffusional inhibition

$$\Phi = (dn/dt)\,(1/c)\,(R^2/D)\,(f_n/f_v) \geqq 0.3 \ldots 3$$

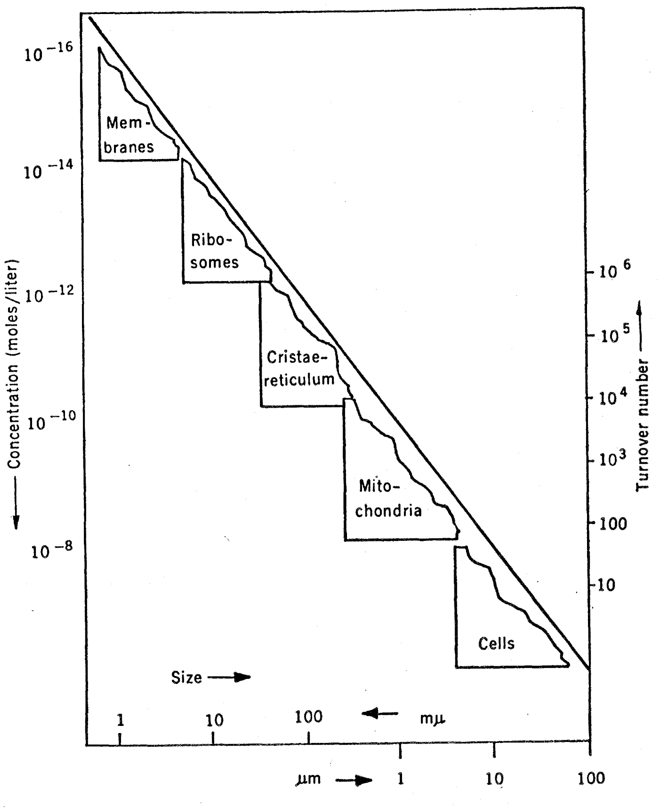
where dn/dt is still the total metabolic rate per unit cell volume, c is the actual concentration of the intermediate at the subunit, f_n is the fraction of the metabolic rate involved in the specific chemical reaction process, and f_v is the fraction of cellular volume occupied by this type of subunit.

Transient Occurrences and Pathology

I mentioned earlier that the natural processes of evolution appear to produce structural reaction units that attain a size which is in proper proportion to the concentration of the chemical reactant it must handle, that is, without overdesign, as defined by the Φ criterion. The one time at which we may expect to find an appreciable deviation from this state, and therefore also appreciable concentration gradients, would be during abnormal or transient conditions, for example, at the onset of reproductive processes. Indeed, Child (*36*) has shown that gradients of oxidative activity (revealed by a special technique with oxidizable dyes) do occur during the initial growth of egg cells, and only then. The gradual decay of these gradients is accompanied by structural changes, such as the migration of the cell nucleus. The upset of the diffusion criterion by excessive chemical activity causes the appearance of gradients, and it is highly plausible that these, in turn, provide the causative force of the structural readjustment.

Injury, or the onset of abnormal pathology, would similarly constitute a transient state that can be expected to produce diffusive gradients, which, in turn, could initiate remedial movements, that is, "healing."

At times, the question has been raised as to how important it actually is to provide an adequate effectiveness factor in a catalytic apparatus, since, it can be argued, desired larger conversion rates could still be obtained by using more catalyst, or by increasing the temperature a few degrees. We have already mentioned some of our experiences which show that penalties of some sort arise in nearly all cases



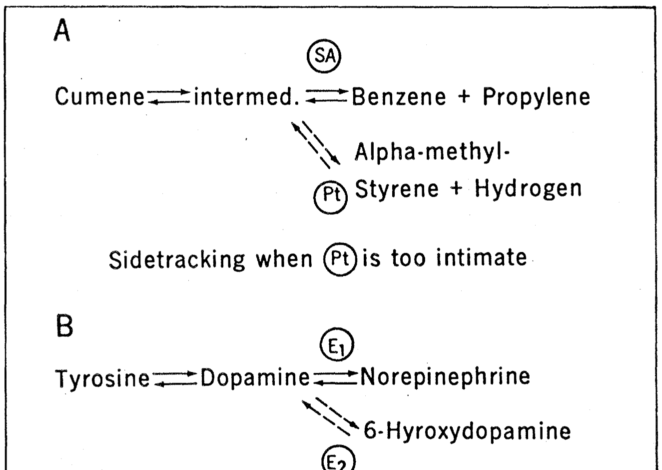


Fig. 10 (left). Maximum allowable size of the catalytic apparatus in a living cell, if it is to process an intermediate species existing at given low concentrations, for the typical reaction rate of cellular oxygen metabolism [after Wiesz (*35*)]. Fig. 11 (right). (A) Sidetracking of the cumene reaction caused by diffusion interception by another catalyst species. (B) Example of sidetracking in a biochemical reactive sequence. (*SA*, silica-alumina particles; *Pt*, platinum-bearing alumina; E_1 and E_2, enzymes 1 and 2.)

of diffusion inhibited operation. The use of additional catalyst to overcome low effectiveness implies wastefulness in material or space (or both). In the biological system, increasing the temperature is not permissible. It upsets the normal relationship of the rates of the many simultaneous processes.

Few, if any, reaction processes, biological or industrial, consist of pure, single-step transformations. There are side reactions and there are consecutive secondary reactions. If one wishes to attain high selectivity for a desired process or ratio of processes, one is greatly constrained in freedom to choose reaction conditions, especially temperature. This, in fact, illustrates the important role of the effectiveness factor and, therefore, of the magnitude of Φ in determining the *selectivity* behavior of a catalytic system.

When reaction intermediates and various catalytic functions are involved, dramatic alterations of selectivity can result from variations in the degree of diffusional coupling between the individual catalytic components. An example is the diversion of the normal reaction path by "diffusion interception." My colleagues Prater and Wei (see *33*) were studying the seemingly simple reaction of cumene to benzene and propylene on silica-alumina particles (Fig. 11A). They discovered that in this reaction, a very low concentration intermediate X is made which could be intercepted and diverted to produce a different set of products. When they interspersed 5-μm particles of platinum-bearing catalyst with 5-μm silica-alumina particles, the normal reaction path was sidetracked to produce α-methylstyrene and hydrogen. A less intimate interdispersion of the same amounts of the two catalyst components, such as the use of millimeter-sized component particles does not produce this result. The Φ criterion defines the conditions of effective interception. It becomes a criterion for intimacy.

The importance of the question of intimate physical *location* of catalysts is again best appreciated in a life system, where sidetracking or alteration of metabolic reaction sequences may mean life or death, or normalcy or disease. This can be illustrated by an example from recent research in chemical neurophysiology. Stein and Wise (*37*) have suggested that a dopamine intermediate in the neurochemistry of norepinephrine production can be shunted away by hydroxylation to 6-hydroxydopamine (Fig. 11B). This material is suspected of causing neural damage, perhaps giving rise to some of the aspects of schizophrenic abnormalcy, if there occurs either a shortage of concentration in enzyme E_1, or an excess of enzyme catalyst E_2. It will be apparent from our experiences and discussion that an alternative explanation may be valid. The result could be produced by the presence of *normal* concentrations of both enzymes but a structural defect in the size or location of portions of the enzymatic apparatus. Structural deficiencies in the neurocellular organization may couple E_1 too loosely, or E_2 too firmly, to the enzymatic sites of the remaining reaction steps. Thus, a defect in structural physiology can cause abnormal overall chemical physiology, although the chemistry of the individual subunits cannot be faulted.

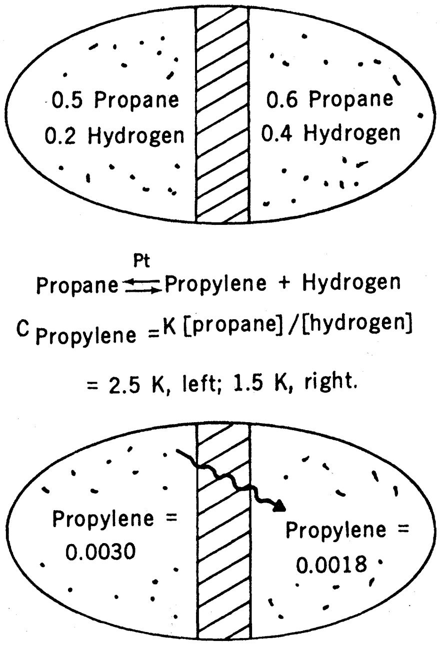


Fig. 12. A model of active diffusion. Propane and hydrogen are placed on either side of an olefin permeable membrane, at the relative concentrations indicated in the upper oval. Platinum catalyst contained on both sides can produce propylene in near thermodynamic equilibrium concentrations. Propane and hydrogen gradients are downward from left to right (lower oval). Net propane transport against its gradient will result.

I have used this as an example only to illustrate how sidetracking can occur in cellular biochemistry, and how the Φ criterion provides a mechanistic and quantitative rationale for it. It must be involved in the interaction of structural and chemical factors in numerous reaction sequences, such as in the studies of the "topography related to the coupling factors in oxidative phosphorylation," discussed by Racker (*38*).

Active Diffusion

Our work on polystep hydrocarbon conversion via minute concentrations of olefin intermediates suggested a simple illustrative model for the long-mysterious phenomenon of active diffusion, of diffusion of a molecular species against its concentration gradient. Figure 12 is a diagram of mixtures of different concentrations of propane and hydrogen being separated by a membrane selectively permeable only by an olefin. The concentration of each compound increases from left to right.

Let there be catalytic material such as platinum in both chambers. We know that even at low temperature platinum catalyzes the dehydrogenation-hydrogenation reaction between propane and propylene; at equilibrium a very small concentration of propylene is created. The ratio of the reactant concentrations is such that although the propylene concentrations will be mi-

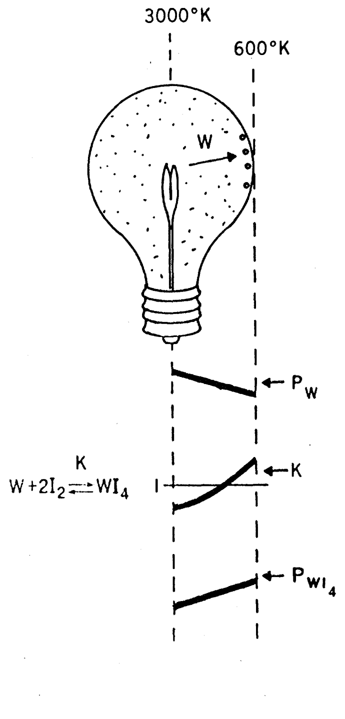


Fig. 13. The iodine lamp, a commercialized model for active diffusion. Tungsten tetraiodide is formed at the cold wall and decomposed at the hot filament. Net transport of tungsten back to the filament and against its gradient is thus accomplished.

nute, they will be lower on the right-hand side. Thus, propylene will diffuse, according to classical laws, down its concentration gradient, from left to right. The net result will be a migration of propane from left to right, that is, against its apparent gradient. The back-and-forth transition of the hydrocarbon between its alkane and alkene form is analogous to the involvement of a "high-energy bond" frequently invoked by the biochemist to explain a driving force. The model illustrates how active diffusion results from the coupling of two normal chemical reactions with the normal, classical downward diffusion, of a chemical intermediate present in very low concentrations. It is not difficult to find corresponding mechanistic steps in a variety of biochemical, aqueous, and ionic reaction conditions. Examples are the proposed "ionophores" (*39*) analogous to the low concentration olefin, and the shift in the equilibria of the back-and-forth reaction that can result from shifts in *p*H (*40*) through the action of additional reactions.

At least one form of activated diffusion in inorganic chemistry has not only been demonstrated, but has been commercialized in a device known as the iodine lamp (*41*) (Fig. 13). The hot tungsten filament produces a relatively high vapor pressure of tungsten, whose atoms diffuse to the cold glass wall. There, its slow accumulation darkens the glass and reduces the useful life of the bulb. The inventors of this device introduced a trace of iodine vapor. In the area of low temperature of the walls, the chemical equilibrium is favorable for formation of tungsten iodide. Decomposition of tungsten iodide occurs at the hot filament. In this way, a gradient of tungsten iodide is running downward and back toward the filament. Tungsten is actually transported back, continuously, and apparently up against its gradient.

Phenomena versus Disciplines: A Postscript

We have traced the significance of the competition between molecular reaction and molecular diffusion, as expressed by the Φ criterion, across many disciplines. It is interesting to note how researchers in many branches of the sciences have struggled with problems that arise from a basically common phenomenon, one that does not "belong" to any special discipline. We need to consider how we might best prepare ourselves and our students to understand and to deal with basic phenomena of general applicability. While we continue a healthy trend to erase interdisciplinary boundaries, we must remember that any collection of items as complex as those that constitute human knowledge can only be sensibly stored, managed, or propagated with some unifying structure. Can we find structures that are orderly, basic, and interdisciplinary? Can the teaching of human experience and knowledge be organized around *phenomena*? The diffusion-transformation interaction is but one example of a general phenomenon; there are many others. For example, energy . . . feedback . . . zero . . . kinetic interection of assemblies . . . each represents a general concept or phenomenon that has meaning, implications, and applicability across an enormous sector of experiences and disciplines, physical, biological, social, physiological, medical, psychological, and others. Furthermore, each can be experienced, enjoyed, and understood in some form at nearly every stage of educational development.

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